REMARKS

Applicants respectfully request reconsideration and withdrawal of the outstanding Office Action rejections in view of the foregoing amendments and following remarks. Claims 28-30, 34, 35, 37, 40, 44-48 and 53 have been amended to place the claims in better condition for examination and to place the claims in conformance with standard U.S. practice. Claim 28 has been amended to include specific phenylalanine compounds of general formula I. Support for this amendment can be found in the present specification at pages 5-11. New claims 54-56 have been added, which incorporate limitations from claims 50-52, whereby claims 50-52 have been cancelled. Support for new claims 54-56 can be found in the present specification at page 11, line 37 to page 12, line 11 and at Example 4. No new matter has been added.

Claims 34, 35, 37 and 53 stand rejected under 35 U.S.C. § 112, second paragraph. Applicants respectfully submit that these claims now satisfy the requirements of 35 U.S.C. § 112, second paragraph.

With respect to claims 34, 35 and 37, the phrases "such as" and "for example" have been removed and a space has been inserted between "phospholipids" and "selected" in claim 34. With respect to claim 53, the claim has been amended to place the claim in conformance with standard U.S. practice. Accordingly, Applicants respectfully request withdrawal of this Office Action rejection.

Claims 28-37, 41-48 and 50-53 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over WO 00 04954 (English language equivalent is US Published Application 2003/0013723). Applicants note that WO 00 04954 is a German language

document and Applicants have based remarks herein on the English language equivalent, U.S. Published Application 2003/0013723. Applicants respectfully submit that U.S. Published Application 2003/0013723 cannot render obvious the present claims for at least the following reasons.

U.S. Published Application 2003/0013723 is directed to 3-amidino phenylalanine derivatives as urokinase inhibitors. It is disclosed at paragraph 0069 of U.S. 2003/0013723 that it is possible to incorporate the 3-amidino phenylalanine derivatives into the membrane of carrier vesicles, i.e., liposomes, to facilitate targeting of active substances enclosed in carrier vesicles. Paragraph 0069 is the only part of U.S. 2003/0013723 that discloses a vesicle or liposome.

Present claim 28 of the instant application requires a liposomal formulation of 3-amidino-or 3-guanidino phenylalanine derivatives. Furthermore, present claim 28 now recites the limitation that the phenylalanine derivatives of general formula I are encapsulated within the liposome. Applicants submit that liposomal encapsulation of the phenylalanine derivatives is distinct from the disclosure of U.S. 2003/0013723, wherein it is possible to incorporate, or embed, the phenylalanine derivatives into the membrane of a carrier vesicle or liposome.

U.S. 2003/0013723 is silent with respect to the encapsulation of the phenylalanine derivatives of general formula I within a liposome. One of skill in the art would recognize from U.S. 2003/0013723 that the phenylalanine derivatives, when embedded in a membrane of a liposome, would serve as a target for lymphocytes. One of skill in the art would also recognize that the present claims require the phenylalanine

derivatives to be an active pharmaceutical ingredient that is encapsulated within a liposome, which is different and distinct from the disclosure of U.S. 2003/0013723.

To further support Applicant's position, Applicants hereby submit an opinion declaration of Wolfgang Schmalix (a co-inventor of the present application) for the Examiner's consideration. This declaration essentially states that one of skill in the art would recognize the therapeutic difference between phenylalanine derivatives embedded in the membranes of liposomes (as described in U.S. 2003/0013723) and phenylalanine derivatives encapsulated by liposomes (as required by the present claims).

Furthermore, administration of the liposomal formulation required by present claim 28 surprisingly leads to prevention of undesirable side effects such as hemolysis and skin irritation that are normally associated with administration of non-liposomal formulations of the same compounds of general formula I. U.S. 2003/0013723 is silent with respect to any reduction in side effects that stems from administration of the formulations disclosed therein. Applicants respectfully direct the Examiner's attention to Tables 3 and 4 and to Example 5 of the present specification for disclosure of such unexpected results. If the Examiner deems it necessary, Applicants would be pleased to submit a Rule 1.132 declaration to confirm such unexpected results arising from administration of liposomal formulations required by present claim 28.

For at least the reasons described above, Applicants submit that the disclosure of U.S. 2003/0013723 cannot render obvious the present claims. Accordingly, Applicants respectfully request withdrawal of this rejection.

Claims 28-32, 41-48 and 50-53 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over WO 00 04954 (English language equivalent is US Published Application 2003/0013723) in combination with Huang et al. (WO 88/09168). Applicants respectfully submit that U.S. Published Application 2003/0013723 in combination with Huang would not lead to a liposomal formulation of the present claims and that Huang does not cure the deficiencies of US 2003/0013723, as discussed above.

As discussed above, US 2003/0013723 cannot render obvious the present claims. US 2003/0013723 is directed to 3-amidino phenylalanine derivatives as urokinase inhibitors wherein it is possible to incorporate the 3-amidino phenylalanine derivatives into the membrane of carrier vesicles, i.e., liposomes, to facilitate targeting of active substances enclosed in carrier vesicles.

Huang is directed to liposomal formulations containing doxorubicin for the treatment of tumors wherein the liposomes contain lechtin, phosphatidylglycerol, cholesterol and a cryoprotectant.

Applicants respectfully submit that the combination of US 2003/0013723 with Huang would lead to a liposome that comprised 3-amidino phenylalanine derivatives embedded in the liposome membrane to facilitate targeting of active substances enclosed in the liposome, as taught in of US 2003/0013723, wherein the liposome would also comprise lechtin, phosphatidylglycerol, cholesterol and a cryoprotectant, as taught by Huang.

Applicants respectfully submit that the combination of US 2003/0013723 with Huang does not lead to the present claims. Furthermore, the liposomal composition of Huang does not cure the noted deficiencies of US 2003/0013723. For at least the above

reasons, Applicants submit that this combination of documents does not and can not render obvious the present claims.

Claims 28-53 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over WO 00 04954 (English language equivalent is US Published Application 2003/0013723) in combination with Barenholz (USP 6,156,337). Applicants respectfully submit that U.S. Published Application 2003/0013723 in combination with Barenholz would not lead to a liposomal formulation of the present claims and that Barenholz does not cure the deficiencies of US 2003/0013723.

As discussed above, US 2003/0013723 cannot render obvious the present claims. US 2003/0013723 is directed to 3-amidino phenylalanine derivatives as urokinase inhibitors wherein it is possible to incorporate the 3-amidino phenylalanine derivatives into the membrane of carrier vesicles, i.e., liposomes, to facilitate targeting of active substances enclosed in carrier vesicles.

Barenholz is directed to liposomal formulations containing DMPG, phosphatidylcholine and cholesterol for delivery of active ingredients. Barenholz further discloses the liposomal formulations disclosed therein are advantageous because of: 1) chemical stability; and 2) better uptake by macrophages.

Applicants respectfully submit that the combination of US 2003/0013723 with Barenholz would lead to a liposome that comprised 3-amidino phenylalanine derivatives embedded in the liposome membrane to facilitate targeting of active substances enclosed in the liposome, as taught in of US 2003/0013723, wherein the liposome would also comprise DMPG, phosphatidylcholine and cholesterol, as taught by Barenholz.

Applicants respectfully submit that the combination of US 2003/0013723 with Barenholz does not lead to the present claims. Furthermore, the liposomal composition of Barenholz does not cure the deficiency of US 2003/0013723. For at least the above reasons, Applicants submit that this combination of documents does not and can not render obvious the present claims.

Claims 28, 31-36, 41-48 and 50-53 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Henkin (USP 6,716,963). Applicants respectfully submit that Henkin cannot render obvious the present claims for at least the following reasons.

Henkin is directed to polypeptide angiogenic drugs that require at least nine amino acid residues therein. Henkin discloses that 1 out of 9 of these amino acid residues can be a guanadino or amidino phenylalanine derivative.

Present claim 28 now requires a liposomal formulation that encapsulates the guanadino or amidino phenylalanine derivatives defined by general formula I. The phenylalanine derivatives defined in general formula I of present claim 28 are not the same as the polypeptide derivatives with at least 9 amino acid residues disclosed by Henkin. Furthermore, Henkin does not teach or suggest the use of individual molecules of guanadino or amidino phenylalanine derivatives in the formulations disclosed therein. Henkin only discloses polypeptides with at least 9 amino acid residues.

Accordingly, Applicants respectfully submit that one of skill in the art would not have used the disclosure of Henkin to arrive at a liposomal formulation encapsulating the guanadino or amidino phenylalanine derivatives of general formula I, as now required by present claim 28.

Claims 33-53 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Henkin (USP 6,716,963) in combination with Barenholz (USP 6,156,337). Applicants respectfully submit that the combination of Henkin and Barenholz does not lead to the present claims and that the disclosure of Barenholz does not cure the deficiency of Henkin.

As discussed above, Henkin is directed to polypeptide angiogenic drugs that require at least nine amino acid residues therein. Henkin discloses that 1 out of 9 of these amino acid residues can be a guanadino or amidino phenylalanine derivative.

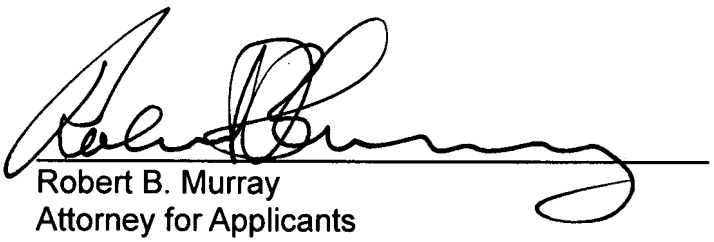
Barenholz is directed to liposomal formulations containing DMPG, phosphatidylcholine and cholesterol for delivery of active ingredients. Barenholz further discloses the liposomal formulations disclosed therein are advantageous because of: 1) chemical stability; and 2) better uptake by macrophages.

Applicants respectfully submit that the combination of Henkin with Barenholz would lead to a liposome that comprised a polypeptide with at least 9 amino acid residues wherein one of the residues may be a guanadino or amidino phenylalanine derivative, as taught in by Henkin, wherein the liposome would also comprise DMPG, phosphatidylcholine and cholesterol, as taught by Barenholz.

Accordingly, Applicants respectfully submit that the combination of Henkin with Barenholz does not lead to the present claims. Furthermore, the liposomal composition of Barenholz does not cure the deficiency of US 2003/0013723. For at least the above reasons, Applicants submit that this combination of documents does not and can not render obvious the present claims.

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and withdrawal of the outstanding Office Action rejections. Early and favorable action is awaited.

Respectfully submitted,

By 

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